

Current Status of Research on Anti-osteoporotic Drug Treatment and Compliance in Patients with Osteoporotic Fractures

Xiaozhen Lin, Yiji Li, Limei Wang*, Qiujiào Liao

Youjiang Medical University for Nationalities, Baise 533000, Guangxi, China

*Correspondence Author

Abstract: *Osteoporotic Fracture (OPF), also known as fragility fracture, is a low-energy, non-violent fracture that commonly occurs in the elderly. Such fractures mostly occur in the thoracolumbar vertebral body, hip, distal radius and other parts, and are the main factors that cause osteoporosis patients to be hospitalized for diagnosis and treatment. Secondary fractures are prone to occur after fractures, and anti-osteoporotic treatment can effectively prevent further fractures in patients with osteoporotic fractures. Due to factors such as patients and their families' insufficient understanding of the necessity of anti-osteoporosis drug treatment after fragility fractures, insufficient awareness of the risk of re-fracture, lack of follow-up management of drug compliance after treatment, and untimely monitoring of anti-osteoporosis efficacy, etc. The treatment initiation rate and medication compliance of anti-osteoporosis drugs in patients with osteoporotic fractures are low. This article systematically reviews the incidence and disease burden of osteoporotic fractures, the understanding of diagnosis, treatment and management of osteoporotic fractures, the status of anti-osteoporotic drug treatment and compliance, and efficacy monitoring of patients after osteoporotic fractures. Provide a reference for establishing effective medication compliance management for OPF patients.*

Keywords: Osteoporotic fractures, Medication, Medication adherence.

1. Introduction

Osteoporotic Fracture (OPF), also known as fragility fracture, is a low-energy, non-violent fracture that commonly occurs in the elderly. This type of fracture mostly occurs in the thoracolumbar vertebral body, hip, distal radius and other parts, and is the main factor causing hospitalization for osteoporosis patients [1]. After a fracture, the patient's activities are limited and bone loss is accelerated; while the fracture damages the bone tissue, the treatment process will also lead to further bone loss, increasing the chance of re-fractures [2]. The results of a 10-year retrospective study of a large sample in Australia showed that 38.2% of OPF patients required readmission for treatment due to recurrent fractures [3]; the research team followed up the results of 586 patients with osteoporotic vertebral fractures in 4 tertiary hospitals in the early stage. It was found that the recurrence rates of osteoporotic vertebral fractures at 1, 2, 3, and 4 years were 18.0%, 28.5%, 38.3%, and 66%, respectively, and the prognosis was poor [4]. One osteoporotic fracture occurs every 3 seconds worldwide [5]. Once a patient suffers an osteoporotic fracture, the risk of another fracture within 1 year is 2.7 times higher than the first fracture [6]. Chinese population aged 60 and over is approximately 264 million, accounting for 18.70% of the country's total population [7]. Patients with osteoporosis fractures are mainly elderly people, and the patient cardinal number is large, requiring precise intervention and management.

The number of patients with osteoporotic fractures who have recurrent fractures is high and the individual differences are large. Accurate identification of patients at high risk of recurrent fractures is conducive to targeted treatment and prevention. There are many existing fracture assessment tools, among which the Fracture Risk Assessment Tool (FRAX) is the most widely used, but this tool is not suitable for assessing patients who have already had fractures. The research team

previously constructed an OPF recurrence prediction model based on a multi-center, large-sample prospective cohort and completed online conversion, but the clinical application effect remains to be tested.

Existing studies have confirmed that drug therapy can significantly improve the osteoporosis condition of OPF patients. Active anti-osteoporosis treatment is an important measure to prevent recurrent fractures in patients with osteoporotic fractures [8]. Literature review shows that "anti-osteoporosis treatment" in China has not received enough attention. There are widespread problems such as low initiation rate of anti-osteoporosis treatment and lack of supervision of standardized treatment. In other words, the prevention of recurrent fractures has not received enough attention. A domestic epidemiological survey showed that only 11.0% of patients took anti-osteoporosis drugs regularly after the first surgery [9]. The previous study of the research team showed that the duration of anti-osteoporosis drug treatment is an influencing factor for recurrent fractures in OPF patients. The longer the drug treatment time, the lower the risk of recurrent fractures [4]. The results of a domestic study on drug initiation and compliance showed that, taking bisphosphonates as an example, the drug initiation rate for OPF men was only 6.76%, while that for women was 15.17%; 6 months after surgery, the drug compliance rate for men was 70.27%, while that for women was 76.97%. 7-12 months after surgery, the rate dropped to 41.89% for men and 57.86% for women [10]. The guidelines recommend that OPF drug treatment should follow a clear duration of medication, generally 3-5 years [11]. Therefore, the management of drug treatment compliance after discharge is crucial.

2. The Incidence and Disease Burden of Osteoporotic Fractures

With the aging of the population and the increase in life

expectancy, the incidence of osteoporotic fractures is generally on the rise. A survey in South Korea based on the Health Insurance Review and Assessment Service (HIRA) database showed that the proportion of osteoporotic fractures gradually increased from 2009 to 2017, an increase of 60% [12]; some scholars predict that from 2017 By 2035, the new incidence rate of osteoporotic fractures in Singapore will increase by 58% [13]. As the population base of OPF increases year by year, the resulting economic burden of the disease increases year by year, placing a heavy economic burden on patients and society. It is predicted that by 2040, the number of osteoporotic fracture patients in Chinese women alone will reach 241.7 million, resulting in a disease burden of US\$997 billion [14]. It can be seen that OPF is a common disease that seriously threatens the healthy life of the elderly. It has the characteristics of high incidence and heavy disease burden. It is necessary to pay attention to the diagnosis, treatment and prognosis management of the disease.

3. Inadequate Understanding of Diagnosis, Treatment and Management of Osteoporotic Fractures

Medical diagnosis and treatment: Since osteoporosis is a hidden disease with a long course, most patients present for pain or fractures as the first reason for their visit. Orthopedics is the first department to receive OPF patients. A survey of 200 orthopedic physicians in tertiary hospitals in central, eastern and southern China showed that 44.1% of orthopedic physicians would refer their OPF patients to internal medicine/osteoporosis/endocrinology departments for treatment to prevent recurrent fractures [15]. In a previous study, the research team conducted a survey of four tertiary hospitals in Baise and Nanning, Guangxi, and found that less than 20% of orthopedic physicians would refer OPF patients to endocrinology departments for treatment, which was far lower than the level reported in the literature. In addition, a survey of physicians in the fields of orthopedics, endocrinology, rheumatology and immunology, and geriatrics showed that for follow-up treatment after fracture healing, 91% of physicians recommended that OPF patients continue to see osteoporosis or endocrinology departments, but only 31% of the physicians' hospitals had long-term treatment plans for OPF [16]. This also suggests that there are large differences in the diagnosis and treatment of OPF in different regions, and the long-term clinical treatment plan for OPF needs to be improved.

Patient cognition: An authoritative survey of OPF patients in the Asia-Pacific region by the International Osteoporosis Foundation (IOF) showed that nearly half of the respondents did not know that fractures were a warning sign of osteoporosis; 40% of the respondents were uncertain or did not believe that they were at risk of fracture again; although 78% of the respondents claimed to know what osteoporosis was, more than 80% believed that bone fragility was a normal aging process; and 29% of the respondents had not discussed fracture prevention with their doctors [17]. The level of cognition directly affects the patient's compliance with treatment. In order to improve patient cognition, it is necessary to establish an effective communication channel between doctors and patients, intuitively inform OPF patients of the risk of recurrent fractures, and conduct effective

education.

4. Initiation Rate and Compliance of Drug Treatment for Osteoporotic Fractures

Drug treatment after osteoporotic fracture can reduce the risk of re-fracture [18, 19]. Although the effect of anti-osteoporotic drug treatment is confirmed, there are still gaps in current clinical treatment. The results of a prospective study in Austria showed that 80% of patients with major osteoporotic fractures did not receive anti-osteoporotic treatment [20]; survey data from South Korea showed that even after osteoporotic fractures, only 41.9% Patients received anti-osteoporosis treatment within the next 12 months [21]; in the United States, less than 25% of women received osteoporosis evaluation and treatment within 1 year after their first hip fracture [22]; The anti-osteoporosis drug treatment rate reported in Fujian, in China the rate is also low, 22.1% for women and only 9.5% for men [23]; Xu Hao et al. conducted a study on 560 patients with fragility fractures. It was found that only 44.5% of elderly patients with fragility hip fractures received osteoporosis treatment during hospitalization, and less than 40% of patients continued anti-osteoporosis treatment after discharge [24]. In summary, the initial rate of patients receiving anti-osteoporosis treatment is generally low. Therefore, there is a need to manage medication compliance in patients initiating anti-osteoporotic fractures.

OPF patients have a high re-fracture rate, and anti-osteoporosis drug treatment is an important factor affecting re-fracture [25]. Poor compliance with anti-osteoporosis drug treatment can increase the incidence of re-fracture, thereby affecting their quality of life and increasing the burden on society and patients' families. Domestic studies have shown that OPF patients who regularly take anti-osteoporosis drugs have a significantly lower incidence of re-fracture after one year than the control group [26]; OPF patients who take anti-osteoporosis drugs (bisphosphonates) can effectively improve their bone density and reduce the incidence of re-fracture [27]. Re-fracture in OPF patients can increase the economic burden of national medical insurance and the burden on families. Foreign studies have shown that by 2029, the New South Wales Health Department is expected to pay a total medical cost of approximately A\$2.4 billion related to elderly re-fractures, which is much higher than in the past decade [28]. Due to the high disability and mortality rates of OPF patients, their ability to take care of themselves after fractures is reduced and they need care, which increases the burden of care for patients' families.

In summary, the treatment rate and compliance of OPF anti-osteoporosis drugs need to be improved to avoid the occurrence of further fractures.

5. Anti-osteoporosis Efficacy Monitoring and Biochemical Indicators

The latest authoritative diagnosis and treatment guidelines issued by my country Chinese recommend monitoring drug efficacy: monitoring serum calcium, phosphorus, alkaline

phosphatase, parathyroid hormone, 25-hydroxyvitamin D and drug safety every 3 months; monitoring liver and kidney function and blood routine every 6 months; monitoring bone density and new vertebral fractures every 12 months. However, such examinations and evaluations are rarely completed in clinical practice [29]. Monitoring the efficacy of anti-osteoporosis drugs can effectively track the effect of drug treatment and provide a reference for clinicians to adjust the use of drugs. At present, the efficacy monitoring methods of anti-osteoporosis drugs mainly rely on surrogate markers, such as bone density and bone metabolism markers. Dual-energy X-ray absorptiometry to measure bone density is the most widely used imaging method for evaluating the efficacy of anti-osteoporosis drugs and is regarded as the "gold standard". However, changes in bone density generally require more than 1 year of anti-osteoporosis treatment to show obvious changes [24]. Due to the long time span, patients do not receive timely feedback on the effect of medication, which in turn affects their medication compliance.

Biochemical indicators of bone metabolism: The indicators commonly monitored in clinical practice include calcium and phosphorus metabolism regulation indicators, hormones and cytokines, bone formation markers, and bone resorption markers. The latter two markers are collectively referred to as bone turnover markers [30]. Clinically, the effects of drug treatment can be evaluated by understanding the levels of calcium and phosphorus metabolism regulation indicators and bone turnover markers to guide anti-osteoporosis treatment. In the process of calcium, phosphorus and bone metabolism regulation, parathyroid hormone, calcitonin and vitamin D₃, osteocalcin, type I procollagen amino-terminal peptide, type I collagen cross-linked C-terminal peptide, etc. are all important evaluation indicators.

(1) Parathyroid hormone (PTH): Synthesized and secreted by the chief cells of the parathyroid gland, it plays an important role in the differentiation, maturation and apoptosis of osteoblasts and osteoclasts; it can promote bone resorption and bone turnover, and make bone calcium enters the blood and increases blood calcium. When bisphosphonates are used clinically to treat osteoporosis, due to the inhibition of osteoclasts, blood calcium decreases, PTH secretion increases, blood PTH slightly increases, and vitamin D synthesis increases [31].

(2) Calcitonin (CT) is an important peptide hormone involved in the regulation of calcium and phosphorus metabolism. It was first discovered by Copp and other researchers in 1961. Its main physiological effect is to reduce the number of osteoclasts and inhibit the activity of osteoclasts. activity, reducing bone resorption.

(3) Vitamin D₃ (vitamin D₃) is a naturally occurring fat-soluble vitamin, a steroid hormone [32], which plays a role in regulating calcium and phosphorus metabolism and bone metabolism. Lack of vitamin D in the human body will lead to accelerated bone metabolism, severe bone loss, and easy risk of osteoporotic fractures [33].

(4) Osteocalcin (bone gamma - carboxyglutamic - acid - containing proteins, BGP) is a specific biochemical marker

that reflects bone formation. Studies have found that the osteocalcin level in osteoporosis patients is significantly lower than that in normal subjects. Clinically, osteocalcin can be monitored to understand osteoblast activity and bone formation, so as to detect the decline in bone formation ability as early as possible and intervene to prevent the occurrence of osteoporosis [34].

(5) The content of type I procollagen amino-terminal peptide (PINP) in serum reflects the ability of osteoblasts to synthesize collagen and can be used to monitor osteoblast viability and basic laboratory indicators of bone formation. PINP has high specificity and sensitivity in predicting the occurrence of osteoporosis, evaluating bone mass, and monitoring anti-osteoporosis efficacy, and is not affected by hormones [35].

(6) Collagen type I cross-linked C-terminal peptide (CTX) reflects osteoclast bone resorption activity, is an important biochemical marker metabolic index of bone resorption, and is the most widely used collagen degradation marker. It is closely related to the degree of bone resorption [36].

In general, OPF has a high incidence and a heavy disease burden, and the risk of re-fracture needs to be identified, the drug treatment rate and compliance need to be improved, and the efficacy monitoring needs to be improved. It is necessary to identify the risk of re-fracture in OPF patients and establish standardized, full-course, and sequential treatment of anti-osteoporosis drugs on this basis to ensure the effectiveness of anti-osteoporosis drug treatment.

Conflict of Interest

The authors have no conflicts of interest to declare.

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Author Profile

Limei Wang (1986-), corresponding author, female, bachelor's degree, postgraduate student, supervisor nurse, research direction: surgical nursing, Youjiang Medical University for Nationalities, email: 869222794@qq.com

Xiaozhen Lin (1990-), first author, female, bachelor, postgraduate student, supervisor nurse, research direction: surgical nursing, Youjiang Medical University for Nationalities, email: 754232140@qq.com

Yiji Li (1996-) Co-first author, female, BSN, postgraduate student, teaching assistant, research direction: surgical nursing, Youjiang Medical University for Nationalities, email: 1852964122@qq.com